

IN THE CLAIMS

1. (currently amended) An isolated nucleic acid molecule comprising a polynucleotide encoding a phospholipase A2 γ polypeptide and configured to generate transgenically generated phospholipase A2 (TGiPLA₂) mice. (~~SEQ ID NO:1~~)

2. (original) An isolated nucleic acid molecule in accordance with Claim 1, wherein said phospholipase A2 γ polypeptide catalyzes cleavage of fatty acids from the sn-2-position of phospholipids.

3. (currently amended) An isolated nucleic acid molecule in accordance with Claim 2 wherein said polynucleotide encodes a sequence as set forth in ~~SEQ ID NO: 1 or SEQ ID NO:2~~ SEQ ID NO: 6.

4. (original) A vector comprising a nucleic acid molecule in accordance with Claim 1.

5. (original) A cell transformed or transfected with a vector in accordance with Claim 4.

6. (withdrawn) An isolated nucleic acid molecule comprising a fragment of a polynucleotide encoding a phospholipase A2 γ wherein said fragment specifically hybridizes with a sequence as set forth in at least one of SEQ ID NOS 3, SEQ ID NO:4 and SEQ ID NO: 5.

7. (currently amended) An isolated nucleic acid comprising a polynucleotide having at least about 90% sequence identity with ~~SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NOS 6, 7, 8 or 9~~ SEQ ID NO: 6 wherein the encoded polypeptide has or modulates enzymatic activity, and wherein the isolated nucleic acid is configured to generate transgenically generated phospholipase A2 (TGiPLA₂) mice.

8. (currently amended)) An isolated nucleic acid according to claim 7 comprising ~~SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NOS 6, 7, 8 or 9~~ SEQ ID NO: 6.

9. (currently amended) An antisense sequence which specifically hybridizes to SEQ ID NO: 3, ~~or SEQ ID NO: 4, SEQ ID NO: 5 or SEQ ID NO: 6,~~ wherein the antisense is configured to generate transgenically generated phospholipase A2 (TGiPLA₂) mice.
10. (withdrawn) An isolated polypeptide comprising a phospholipase A₂γ.
11. (withdrawn) An isolated polypeptide in accordance with Claim 10 which catalyzes cleavage of fatty acids from the sn-2-position of phospholipids.
12. (withdrawn) An isolated polypeptide in accordance with Claim 11 which has at least 90% identity with SEQ ID NO: 1 or SEQ ID NO:2.
13. (withdrawn) An isolated polypeptide in accordance with Claim 12 comprising SEQ ID NO:1 or SEQ ID NO:2.
14. (withdrawn) An isolated polypeptide in accordance with Claim 12 which is a conservatively substituted variant of SEQ ID NO:1 or SEQ ID NO:2.
15. (withdrawn) An antibody capable of binding to a phospholipase A₂γ according to Claim 1.
16. (currently amended) A vector comprising a nucleic acid molecule in accordance with Claim 1 suitable for ~~vectoring into~~ generating a transgenic mouse wherein ~~the reporter a reporter~~ gene encodes an enzyme capable of being detected by a colorimetric, fluorometric or luminometric assay.
17. (currently amended) A ~~method~~ vector in accordance with Claim 16 wherein said reporter gene encodes a luciferase.
- 18- 20. (canceled).
21. (withdrawn) A method for preparing a transgenic mouse which further comprises breeding a transgenic founder mouse having SEQ ID 1 stably integrated in its genome with WT B6CBAE1/J mice.

22. (withdrawn) A transgenic mouse having in its genome a nucleic acid molecule comprising a polynucleotide encoding a phospholipase A₂ γ polypeptide. (SEQ ID NO: 1)

23. (withdrawn) A transgenic mouse in accordance with Claim 22 wherein said phospholipase A₂ γ polypeptide catalyzes cleavage of fatty acids from the sn-2-position of phospholipids.

24. (withdrawn) A transgenic mouse in accordance with Claim 23 wherein said polynucleotide encodes a sequence as set forth in SEQ ID NO:1 or SEQ ID NO:2.

25. (canceled).

26. (withdrawn) A transgenic mouse having within its genome a nucleic acid molecule comprising a fragment of a polynucleotide encoding a phospholipase A₂ γ wherein said fragment specifically hybridizes with a sequence as set forth in SEQ ID NOS:3 or SEQ ID NO:4 or SEQ ID NO:5.

27-31. (canceled).

32. (withdrawn) A mitochondrial import signal and cleavage site (LRK/VS) (SEQ ID NO:95) immediately downstream from the 74 kDa alternative start site which directs iPLA₂ γ into mitochondria resulting in a truncated protein of approximately 72 kDa.

33. (withdrawn) A subcellular localization of iPLA₂ into both peroxisomes and mitochondria which may have important implications for the role of iPLA₂ in modulating cellular function.

34. (withdrawn) An alternative exon 5 splice variant utilizing gt/ag splice junction and resulting in a novel 5 amino acid change (ASCSV) SEQ ID NO:28.

35. (withdrawn) iPLA₂ exons designated exons 1 (SEQ ID NO:29) and 4 (SEQ ID NO:30) corresponding to genomic sequence 135327-135622 and 125460-125571 of GenBank genomic clone RG054D04.

36. (withdrawn) A truncated iPLA₂γ 63kDa (SEQ ID NO: 21) resulting from initiation at methionine number 122 of iPLA₂ which is expressed in the baculoviral and in vitro expression systems at least 20 fold greater (at the mRNA and protein levels) than the full -length 88kDa (SEQ ID NO: 1) protein product.

37. (currently amended) A transgenic construct containing ~~the γMHC promoter a promoter~~ upstream of the full-length iPLA₂ phospholipase A2 (iPLA₂) coding sequence (SEQ ID NO: 6) for myocardial specific expression of recombinant iPLA₂ in TGiPLA₂ transgenically generated phospholipase A2 (TGiPLA₂) mice.

38. (withdrawn) A transgenic mouse (TGiPLA₂) which expresses 77kDa, 74kDa, 63kDa, and 45kDa isoforms of recombinant human iPLA₂.

39. (withdrawn) A polypeptide (SEQ ID NO: 1) with alternative ATG start sites encoding 88, 77, 74, and 63kDa iPLA₂ proteins

40. (currently amended) An in vitro expression construct in ~~which~~ which a truncated iPLA₂ ~~sequences (SEQ ID NO: 6, 15, 18, and 21) are~~ sequence is cloned downstream from the SV40 promoter of ~~vector pEF Invitrogen, wherein the in vitro expression construct is~~ configured to generate transgenically generated phospholipase A2 (TGiPLA₂) mice.

41. (withdrawn) A transcription factor binding region defined by gel shift analysis between nucleotide residues 6-50 encoding the 88 kDa protein and including the sequence 5'-TATTAATCTGACTGTAGATATATATATTACCTCCTTAGTAATGC-3' (SEQ ID NO:59) within the N-terminal coding region of iPLA₂γ.

42. (withdrawn) Three MyoD transcription factor binding sites (E-boxes) defined by the consensus nucleotide sequence CANNTG in promoter 1 (pre exon 1) sequence of the iPLA₂γ gene corresponding to nucleotide residues – thought – corresponding to nucleotide sequence 5'-CAAGTG-3' (SEQ ID NO: 60), -53 through – corresponding to nucleotide

sequence 5'-CAGGTG-3' (SEQ ID NO:61), and – through – corresponding to nucleotide sequence 5'-CAGGTG-3' (SEQ ID NO:62) upstream from start of exon 1.

43. (withdrawn) An initiator (Inr) sequence with a consensus sequence of Py-Py-A-N-T/A-Py-Py at which nuclear protein constituents bind to 5'-GCG TCA CTT CCG CTG GGG GCG G-3' (SEQ ID NO: 77) at nucleotide residues – through – upstream from the putative start of exon 2.

44. (withdrawn) A pre exon 2 sequence 5'-GCCAGTGTTTG-3' (SEQ ID NO: 78) which is consistent with a CORE promoter element was identified in comparisons of human, mouse, and rat sequence.

45. (withdrawn) A transcriptional regulatory domain within the 5' coding region (nucleotide residues 1-315)(SEQ ID NO: 57) of iPLA₂γ.

46. (withdrawn) A nuclear binding domain corresponding to SEQ ID NO:59 defined by gel shift analysis within the transcriptional regulatory domain.

47. (withdrawn) iPLA₂γ exons SEQ ID NO:29 and 30 corresponding respectively to exons 1 and 4.

48. (withdrawn) A novel splice variant X resulting from splicing exon 1 and truncated exon 5 sequence (SEQ ID NO:5).